REMARKS

Applicant requests reconsideration of the application in view of the foregoing amendments and the discussion that follows. The status of the claims as of this amendment is as follows: Claims 1-6 and 37-46 are pending. Claims 7, 8, and 10-24 were previously withdrawn and canceled and Claims 9 and 25-36 were previously canceled. Applicant reserves the right to file divisional applications to the separately patentable subject matter thereof. Claims 1-43 have been canceled herein and claim 44 has been amended herein. Applicant reserves the right to file continuation applications to the subject matter of canceled claims 1-43.

The Amendments

The specification was amended in several paragraphs to reinstate some of the language of the paragraphs prior to the previous amendment thereby addressing certain issues raised in the Office Action.

The paragraph on page 4, lines 20-30 was amended to recite that the sandwich comprises both a receptor having the substrate molecules and a receptor having a label wherein the receptors are in close proximity. Support therefor is in the specification, for example, in the paragraph preceding the above paragraph.

Line 13 on page 4 was amended to recite that the product can then be detected by a second sandwich binding assay using specific binding reagents to provide antecedent basis for the recitation of "the specific binding reagents" in line 14 on page 4.

Line 14 on page 4 was amended to refer to the specific binding reagents required for the second sandwich assay. Support therefor is in the specification, for example, lines 12-13 on page 4.

Claim 44 was amended in the preamble to refer to a method for determining the presence or concentration of an analyte in a medium. Support therefor is in the specification, for example, page 1, lines 7-8, and page 56, lines 13-17. Claim 44 was amended to recite that the substrate comprises digoxigenin-linked biotin linked to the support through a reactive oxygen cleavable linker. Claim 44 was also amended to recite that the amount of released digoxigenin-linked biotin is related to the amount of

analyte in the medium. Support therefor is in the specification, for example, page 60, lines 4-5, and page 56, lines 13-17.

Objection to the Specification

Applicant submits that the foregoing amendments to the specification obviate the objections with regard to alleged introduction of new matter and to certain of the informalities raised in the Office Action. Asserted informalities not specifically addressed by amendment are discussed below.

The Office Action asserts that the mechanism by which release of the substrate with formation of a first binding site may be accompanied by unmasking of at least some of a second binding site is unclear. The specification indicates that, in one embodiment of the invention, an oxidant cleavable linker may be used to attach to a support a substrate molecule having two binding sites wherein one of the binding sites is at least partially masked and is completely unmasked upon cleavage of the link and formation of the product. Masking is described in the specification as a situation whereby the functional group is unable to bind to its specific binding reagent. Such masking can arise simply by virtue of the substrate being bound to a surface. For instance, as set forth in the specification, the substrate may be bound within pores of the support or surface, i.e., an agarose gel, where the pores are too small to accommodate the specific binding reagent. Alternatively, numerous substrate molecules bound to a relatively smooth surface will be unavailable for binding to a specific binding reagent provided that the specific binding reagent is sufficiently bulky as, for example, when it is attached to latex particles. Thus, release of the substrate with formation of the first functional group or binding site may be accompanied by unmasking of at least some of the second functional group or binding site.

Particular examples of unmasking are also set forth in the specification. For example, the specification discusses a method for the selective protection or masking of biotin and analogues thereof at the ureido nitrogen using a singlet oxygen cleavable group. The method employs a copper catalyzed coupling reaction to couple the ureido nitrogen of biotin with a variety of unsaturated singlet oxygen sensitive compounds such as oxazole and anthracene halides, vinyl halides, and aryl halides. Deprotection or

demasking of the biotin is accomplished in the presence of singlet oxygen, which cleaves off the masking group. The cleavable group may function as a protective mask to shield biotin in the presence of proteins such as avidin and streptavidin, which strongly bind to biotin. Alternatively, the cleavable group may function simultaneously as a linker to attach biotin to a molecule, support or surface and as a protective mask to shield the biotin in the presence of binding proteins. Singlet oxygen cleavage of the cleavable group simultaneously frees the biotin from the support or surface and unmasks the biotin, allowing the unmasked biotin to bind to an appropriate protein as desired.

Rejection under 35 U.S.C. 112

Claims 1-6 and 37-46 were rejected under the first paragraph of the above code section as failing to comply with the written description requirement. The Office Action contends that the claims contain subject matter, which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention. Specifically, the Office Action referred to several of the claim limitations as not having antecedent support in the specification as originally filed.

The cancellation of claims 1-6 and 37-43 renders the rejection of those claims under the above code section moot. Cancellation of these claims, however, should not be viewed as acquiescence in the arguments presented in the Office Action.

Claim 44 was rejected under the first paragraph of the above code section with regard to the claim limitation "substrate comprising digoxigenin-linked biotin linked to the substrate through a reactive oxygen cleavable linker." Applicant believes that the amendment to claim 44 obviates this ground of rejection.

Applicant wishes to point out that it has been held that language for an amendment to a claim does not require literal support in an applicant's specification. Rather, it is sufficient if the originally filed disclosure would have conveyed to one having ordinary skill in the art that an applicant had possession of the concept of what is claimed. See, for example, Ex parte Parks, 30 USPQ 2d 1234 (B.P.A.I. 1994). Furthermore, the drawings and originally filed claims as well as the specification may be

relied on to provide a basis for the written description of the invention. Vas-Cath, Inc. v. Mahurkar, 935 F.2d 1555, 19 USPQ 2d 1111 (Fed. Cir. 1991). In the present situation Applicant's specification is sufficient to convey to one having ordinary skill in the art that an applicant had possession of the concept of what is claimed in present claims 44-46.

Claims 1-6 and 37-46 were rejected under the second paragraph of the above code section as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The cancellation of claims 1-6 and 37-43 renders the rejection of those claims under the above code section moot. Cancellation of these claims should not be viewed as acquiescence in the arguments presented in the Office Action. Applicant's comments below apply equally to the rejections of these claims.

Applicant submits that amendments made to claim 44 above obviate the rejection of claim 44 under the second paragraph of the above code section. Applicant offers the following observations with regard to certain of the assertions made in the above rejection.

The Office Action contends that, in claim 44, the recitation of the term "substrate" is indefinite because Applicants' specification appears to use the term "substrate" interchangeably with "product" and "surface." Applicant submits that the above terms are definite in view of the discussion and examples in the specification. The discussion below refers to the example in the specification for digoxigenin-linked biotin as a releasable product. This example assists in showing the relationship between the substrate attached to a surface or support and the detectable product attached to the substrate by a cleavable linker where cleavage of the cleavable linker releases detectable product from the support.

Referring to Fig. 5, by way of illustration and not limitation, it is clear that substrate A-B-D, attached to a support represented by a bead in the figure, is cleaved by singlet oxygen to release detectable product B-D from the support. The particular identities of A and B-D are set forth in the examples, particularly Example 5. The substrate comprises both entity A as the cleavable linker and entity B-D as the releasable product. As indicated in the example, activation of the cleavable linker results

in cleavage of a bond linking product B-D to entity A. The result is release of product B-D leaving a residue of A attached to the support.

As explained in the specification (page 37, line 21, to page 38, line 14), there are a number of groups that can be used in the cleavable link of the substrate that will react with singlet oxygen with release of the product. Oxazoles are particularly attractive because they are quite stable. Reaction with singlet oxygen yields an active ester that will spontaneously hydrolyze or react with an added nucleophilic compound. The reactions lead to the release of groups attached to the oxazole. Examples of other cleavable linkers are indicated in the specification and include, for example, 2,3-disubstituted dioxenes, thioxenes, oxazines, thiazines, dithienes and anthracenes, which react with singlet oxygen to produce diesters that can hydrolyze or react with an added nucleophile. In either event, the result is a cleaved portion and a residual portion of the cleavable linker. Thus, in many of the cleavable linkers that form part of the substrate along with the product that is to be released, a bond linking the product to the cleavable linker is broken releasing the product from the remainder of the cleavable linker. As mentioned above, the cartoon representation in Fig. 5 illustrates this by showing the action of singlet oxygen on the cleavable linker A, which releases product B-D and leaves behind a residue of A still attached to the support. The nature of the cleavable linker determines whether or not there is a residual portion of the linker that remains after release of the product. Thus, depending on the nature of the cleavable link, which may be a compound or simply a bond, the released product may be a portion of the substrate or essentially the entire substrate.

Rejection under 35 U.S.C. 102

Claims 1, 2 and 4-6 were rejected under paragraph (e) of the above code section as being anticipated by Singh, *et al.* (U.S. Patent No. 6,770,439) (Singh). Without acquiescing in any way with the arguments, and the response to Applicant's arguments, presented in the Office Action, the cancellation of claims 1, 2 and 4-6 renders the above rejection moot.

Rejection under 35 U.S.C. 103

Claims 3 and 37-43 were rejected under paragraph (a) of the above code section as being unpatentable over Singh in view of Oh and Steinberg (U.S. Patent No. 5,851,77) (Oh). Without acquiescing in any way with the arguments, and the response to Applicant's arguments, presented in the Office Action, the cancellation of claims 3 and 37-43 renders the above rejection moot.

Conclusion

Applicant has demonstrated that claims 44-47 satisfy the requirements of 35 U.S.C. 112. The Office Action indicated that claims 44-47 appeared to be free of the prior art. Furthermore, the specification is free of informalities as discussed above. Allowance of the above-identified patent application, it is submitted, is in order. In any event, Applicant requests entry of the above amendments because they narrow the number of issues and place the application in better form for consideration on appeal.

Respectfully submitted,

Theodore J. Leitereg
Attorney for Applicant
Reg. No. 28,319

Theodore J. Leitereg
31420 Pennant Ct.
Temecula CA 92591
(602) 369-1751